Parasitic Central Nervous System Infections in Immunocompromised Hosts

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Immunosuppression due to therapy after transplantation or associated with HIV infection increases susceptibility to various central nervous system (CNS) infections. This article discusses how immunosuppression modifies the presentation, diagnosis, and treatment of selected parasitic CNS infections, with a focus on toxoplasmosis, Chagas disease, neurocysticercosis, schistosomiasis, and strongyloidiasis.

Immunosuppressive therapy reduces cell-mediated immunity to prevent transplant rejection and graft-versus-host disease (GVHD), but it concomitantly increases the risk of infection due to fungi, viruses (especially herpesviruses), bacteria, and parasites. CNS infection occurs in 5%–10% of transplant recipients and most often manifests as brain abscess, encephalitis, or meningitis [1, 2]. The risk of CNS infection varies with the type of organ transplanted, and, among bone marrow transplant (BMT) recipients, infection is more common after allogeneic than autologous transplantation [3]. Aspergillus fumigatus, Listeria monocytogenes, and Cryptococcus neoformans are the most common causes of posttransplantation CNS infections, but immunosuppression also increases the risk of acquiring parasitic CNS infections and can increase the severity of these infections (table 1).

A patient’s susceptibility to CNS infection after transplantation changes over time [13, 14]. During the initial month after transplantation, CNS infection is most often due to common bacterial pathogens or opportunistic pathogens present in the environment or host (e.g., Aspergillus species and Mycobacterium tuberculosis). Immunosuppression is most pronounced from month 1 to month 6, and CNS infection during this period is most often due to herpesviruses, especially cytomegalovirus and Epstein-Barr virus (EBV); fungi; or atypical bacteria. Parasitic CNS infection most often occurs during this period, with Toxoplasma gondii being the most common infecting organism [15]. Six months after transplantation, immunosuppression therapy is reduced, and CNS infection becomes less common. Patients who require continued high levels of immunosuppressive therapy because of graft rejection or GVHD are at the highest risk of developing an opportunistic CNS infection.

In HIV-infected people, the risk of CNS infection varies with the CD4+ cell count, with the highest risk at a CD4+ cell count of <200 cells/mm³. Focal brain lesions develop in up to 19% of patients with AIDS [16]. The majority of opportunistic CNS infections are due to T. gondii, EBV (primary CNS lymphoma), JC virus (progressive multifocal leukoencephalopathy), and C. neoformans. Parasitic infections, aside from toxoplasmosis, are most commonly found in HIV-infected people from developing countries but are increasingly common in HIV-infected people who travel internationally.

Acute and chronic manifestations of parasitic CNS infection in the immunocompromised host often vary from the manifestations in the immunocompetent host and depend mainly on which CNS site is affected. Neurologic symptoms during chronic infection are frequently due to mechanical obstruction, invasion of vasculature, or enlarging-mass effect. The clinical manifestations and neuroimaging findings for HIV-infected people often differ from those for transplant recipients, presumably because of a selective loss of CD4+ cells during HIV infection, rather than the global immunosuppression due to therapy after transplantation (table 2). Regardless of the host immune status, several host barriers must be breached for a parasite to enter the CNS. Once inside a human host, parasites may immediately cause symptoms or may remain undetected for years. Local tissue damage produced by migrating or grow-
Table 1. Transplantation types and the parasites associated with post-transplantation infection.

<table>
<thead>
<tr>
<th>Type of transplantation</th>
<th>Associated parasite(s)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>Strongyloides stercoralis</td>
<td>Heart transplant recipients are at a higher risk of perioperative cerebrovascular events</td>
</tr>
<tr>
<td></td>
<td>Toxoplasma gondii</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Trypanosoma cruzi</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>T. gondii</td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>Schistosoma species</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T. cruzi</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T. gondii</td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td>Schistosoma species</td>
<td>Renal transplant recipients with schistosomiasis require higher doses of cyclosporine</td>
</tr>
<tr>
<td></td>
<td>S. stercoralis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Taenia solium</td>
<td></td>
</tr>
<tr>
<td>Bone marrow</td>
<td>Schistosoma species</td>
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</tr>
<tr>
<td></td>
<td>S. stercoralis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T. cruzi</td>
<td></td>
</tr>
</tbody>
</table>

NOTE. Compiled from [4–12].

ing parasites can induce marked inflammatory responses, but, in patients with chronic infection or suppressed immune systems, the inflammatory response may be blunted and the clinical manifestations may be minimal [32, 33].

The evaluation of neurologic symptoms in an immunosuppressed host should be guided by (1) the type of transplantation or the CD4+ cell count; (2) the time since transplantation and the receipt of immunosuppressive therapy (for transplant recipients); (3) the serologic status with respect to T. gondii, C. neoformans, and parasites (with evaluation directed by the travel and exposure history of the host); (4) concomitant systemic symptoms (especially pulmonary and gastrointestinal symptoms); and (5) neuroimaging findings (table 2). Eosinophilia in CSF or blood may be absent during parasitic CNS infection, especially during chronic infection [34]. Pulmonary infection usually precedes or accompanies CNS infection with A. fumigatus, C. neoformans, Nocardia asteroides, M. tuberculosis, and endemic mycoses [14, 35].

TOXOPLASMOsis

Felines are the definitive hosts of T. gondii and excrete infectious oocysts in feces [4]. Humans acquire T. gondii infection most often by ingestion of oocysts in contaminated soil or food or bradyzoites in undercooked meat but can also acquire infection via mother-to-fetus transmission, blood transfusion, or organ transplantation [4, 36]. After ingestion of an oocyst, the parasitic organism invades the intestinal epithelium, disseminates throughout the body, encysts, and remains dormant in any nucleated cell. In the United States, 10%–40% of people have latent infection with T. gondii, which is determined by the presence of serum anti-toxoplasma IgG antibodies [37, 38]. The prevalence of people with anti-toxoplasma IgG antibodies in the general population in Chile and France is 80% [39].

In transplant recipients, toxoplasmosis occurs by reactivation of latent infection or is a primary infection if a donor organ containing encysted T. gondii was transplanted into a seronegative recipient [40]. Patients who are seronegative for T. gondii and receive allografts, especially cardiac allografts, from seropositive donors are at the highest risk of developing toxoplasmosis after transplantation [5, 40]. BMT recipients are also at a high risk of developing toxoplasmosis, with up to 70% of recipients developing infection after mismatched allogeneic BMT [6]. Of 3803 bone marrow allograft recipients evaluated in Seattle, 15% were seropositive for T. gondii, and 2% of these seropositive patients later developed toxoplasmosis [41]. Other populations at an increased risk of developing symptomatic T. gondii infection include people receiving blood products or chemotherapy for blood dyscrasias [42–44].

In people with AIDS, toxoplasmosis is most often due to the reactivation of latent infection. One-third of HIV-infected people with serum anti-toxoplasma IgG antibodies develop toxoplasma encephalitis. The absence of serum anti-toxoplasma IgG or IgM antibodies does not exclude the diagnosis of toxoplasma encephalitis, since 22% of people with biopsy-confirmed toxoplasma encephalitis do not have IgG antibodies, and IgM antibodies are rarely present [45, 46]. The incidence
Table 2. Neurologic symptoms and neuroimaging findings in immunosuppressed hosts with parasitic CNS infections.

<table>
<thead>
<tr>
<th>Infecting parasite</th>
<th>Neurologic symptoms</th>
<th>Neuroimaging findings</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Toxoplasma gondii</strong></td>
<td>Headache; cognitive changes; seizures; focal neurologic deficits, such as hemiparesis, ataxia, and facial weakness</td>
<td>Solitary or multiple round ring-enhancing or homogeneously enhancing lesions, usually located at the hemispheric gray-white junction, in the deep white matter, or in the basal ganglia; MRI is more sensitive and may detect multiple lesions not seen on CT scan. Edema is usually present.</td>
<td>Lesion enhancement and perilesional edema may be decreased or absent after transplantation and are inversely correlated with the degree of immunosuppression.</td>
</tr>
<tr>
<td><strong>Trypanosoma cruzi</strong></td>
<td>Headache; cognitive changes; seizures; tremor; hemiparesis</td>
<td>Large solitary or multiple ring-enhancing lesions with surrounding edema</td>
<td></td>
</tr>
<tr>
<td><strong>Taenia solium</strong></td>
<td>Cognitive changes; meningismus; tremor; diplopia</td>
<td>Calcified or homogeneously or ring-enhancing lesions; large cysts. Scolex may be seen on MRI.</td>
<td>Disseminated infection has been reported after transplantation.</td>
</tr>
<tr>
<td><strong>Schistosoma species</strong></td>
<td>Cauda equina (lower-back pain, perineal sensory dysfunction, and bladder or bowel dysfunction) or conus medullaris syndrome (above symptoms with Babinski’s sign or other upper motor neuron dysfunction); transverse myelitis</td>
<td>Solitary or multiple hyperdense lesions in brain or spinal cord. “Arborized” enhancement pattern may be seen on MRI. Surrounding edema and granuloma formation is less common in immunosuppressed hosts.</td>
<td></td>
</tr>
<tr>
<td><strong>Strongyloides stercoralis</strong></td>
<td>Headache; cognitive changes; meningismus; transverse myelitis; hemiparesis</td>
<td>Brain abscess or mycotic aneurysm</td>
<td>Meningitis due to enteric bacteria is common during hyperinfection.</td>
</tr>
</tbody>
</table>

**NOTE.** Compiled from [10, 17–31].
of toxoplasma encephalitis is reduced among people receiving trimethoprim-sulfamethoxazole or dapsone/pyrimethamine therapy as prophylaxis against Pneumocystis carinii pneumonia [47, 48].

Clinical manifestations of CNS toxoplasmosis are similar for transplant recipients and HIV-infected patients and typically include headache, altered mental status, seizures, focal neurologic deficits, hemiparesis, ataxia, and/or facial weakness [2, 14]. Although uncommon, toxoplasmosis of the spinal cord has been reported in transplant recipients and HIV-infected patients [49, 50]. Unlike HIV-infected patients, who reveal a marked ring-enhancement pattern noted on neuroimages, transplant recipients often show a variable enhancement pattern on neuroimages, with the lesion enhancement inversely correlated with the severity of immunosuppression [17, 51].

Definitive diagnosis requires the identification of tachyzoites in biopsy samples, but identification of anti–T. gondii antibodies by ELISA is a sensitive and specific method. Although PCR assay of CSF is highly specific and sensitive in some laboratories, its sensitivity varies by laboratory and technique, and PCR assay should not be used to exclude the diagnosis of toxoplasmosis [52]. The presence of multiple ring-enhancing lesions in the basal ganglia or cerebrum on neuroimages, especially in the presence of anti-toxoplasma IgG antibodies, is suggestive of CNS toxoplasmosis and is sufficient to start presumptive treatment for CNS toxoplasmosis.

Regardless of the host immune status, drug treatment for CNS toxoplasmosis should include pyrimethamine, sulfadiazine, and folinic acid (table 3). Prophylactic treatment with trimethoprim-sulfamethoxazole for 6 months for heart and liver transplant recipients reduces the risk of infection by T. gondii, as well as infection by L. monocytogenes, N. asteroides, and P. carinii [63, 64]. Heart transplant recipients seropositive for T. gondii are at a greater risk of developing toxoplasmosis and are typically prescribed higher dosages of trimethoprim-sulfamethoxazole than are other transplant recipients [65]. In patients with AIDS, treatment does not eradicate T. gondii, so lifelong suppressive therapy is necessary to avoid relapse—unless the patient’s CD4+ cell count rises to >200 cells/mm³ with HAART [66, 67].

**AMERICAN TRYPANOSOMIASIS (CHAGAS DISEASE)**

Trypanosoma cruzi is endemic in most South and Central American countries, but, with the increase in urbanization and emigration, it has spread to the United States and other parts of the world [68, 69]. T. cruzi infection is most often acquired from the bite of a reduviid bug, but it can also be transmitted through the placenta, by ingestion of an infected guinea pig, by blood transfusion, or by organ transplantation [70, 71]. In the United States, tourists and immigrants were previously at the highest risk of acquiring T. cruzi infection but have been superseded by immunosuppressed hosts [18]. Although blood-bank screening has reduced the prevalence of trypanosome-infected transfusions in many South American cities, they are still common. Latin American countries routinely screen tissue for T. cruzi prior to transplantation; the United States has not yet adopted this practice [72]. Chagas disease has been reported in heart, kidney, liver, and BMT recipients, but solid-organ recipients are at the highest risk of acquiring infection [7–9]. In the HIV-infected host, Chagas disease most often reactivates in the CNS, usually when the patient’s CD4+ cell count is <200 cells/mm³, but the disease has been reported in a patient with a CD4+ cell count of 382 cells/mm³ [53, 73].

Acute manifestations of the infection in the immunocompetent host include malaise, myalgia, headache, asthenia, and anorexia [74]. A progression from an acute generalized febrile illness to a chronic symptomatic infection occurs in <5% of people infected with T. cruzi [75]. Chronic infection can produce cardiac failure, megacolon, or megaesophagus; in Brazil, Chagas disease is the primary cause of cardiac failure in men aged <40 years [75, 76]. Meningoencephalitis is the most common CNS manifestation of chronic infection in immunocompetent hosts but usually occurs only in children [77]. CNS mass lesions have not been reported in immunocompetent hosts. In the immunosuppressed host, CNS manifestations occur more frequently and can include meningoencephalitis or a brain mass [19, 78]. Neurologic symptoms depend largely on the number, size, and location of the lesion(s) and may include headache, fever, cognitive changes, seizures, tremor, or hemiparesis [18, 20]. In patients with AIDS, aphasia is also frequently noted [21].

Diagnosis is confirmed by direct observation of intracellular trypomastigotes in serum or CSF [79]. Serum antibody detection tests are sensitive and specific for both acute and chronic forms of T. cruzi infection [80]. Neuroimages of the brain typically show ≥1 ring-enhancing lesions involving both gray and white matter [19].

The initial treatment of CNS chagasic mass lesions in an immunosuppressed host should include benznidazole or nifurtimox therapy [54]. After resolution of the CNS lesion, some experts recommend that HIV-infected patients receive lifetime secondary prophylaxis therapy with benznidazole [55]. Prophylactic therapy for transplant recipients is controversial; parasitemia and reactivation in BMT recipients who have chronic Chagas disease have been successfully controlled with a daily dose of benznidazole, and, in heart transplant recipients, with nifurtimox therapy [7, 56]. Acute Chagas disease in seronegative recipients of kidneys from seropositive donors has been prevented with 2 weeks of benznidazole therapy [81].
<table>
<thead>
<tr>
<th>Infecting parasite</th>
<th>Posttransplantation infection</th>
<th>HIV-associated infection</th>
<th>Suppressive therapy</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxoplasma gondii</td>
<td>Pyrimethamine, 25–100 mg/day for 3–4 weeks, and sulfadiazine, 1.5 g q.i.d. for 3–4 weeks</td>
<td>Pyrimethamine, 200 mg loading dose, then 75 mg/day; sulfadiazine, 6–8 g/day divided q.i.d.; folinic acid, 10–25 mg/day; then pyrimethamine 25–75 mg/day, sulfadiazine, 2–4 g/day, and folinic acid, 10 mg/day</td>
<td>For seropositive HIV-infected patients: TMP-SMZ, 1 double-strength tablet daily, unless CD4 cell count rises to &gt;200 cells/mm³. For heart/liver transplant recipients: TMP-SMZ, 1 single-strength tablet daily or 1 double-strength tablet 3–7 times/week.</td>
<td>Alternative antibiotics for sulfa-allergic patients include clindamycin, azithromycin, and atovaquone; alternative suppressive antibiotics include atovaquone, and dapsone plus pyrimethamine</td>
</tr>
<tr>
<td>Trypanosoma cruzi</td>
<td>Benznidazole, 5 mg/kg/day b.i.d. for 60 days, or nifurtimox, 10 mg/kg/day either t.i.d. or q.i.d. for 120 days</td>
<td>Benznidazole, 5 mg/kg/day b.i.d. for 60 days, or nifurtimox, 10 mg/kg/day either t.i.d. or q.i.d. for 120 days</td>
<td>Benznidazole or nifurtimox, 5 mg/kg 3 times/week. For seropositive transplant recipients, a higher initial dose may be more effective (i.e., nifurtimox, 120 mg/day for 120 days, then 150 mg every other day).</td>
<td>The best pre- and posttransplantation treatment has not been determined and may vary by organ transplanted</td>
</tr>
<tr>
<td>Taenia solium</td>
<td>Albendazole, 15 mg/kg/day b.i.d. (maximum, 400 mg b.i.d.) for 8–30 days, or praziquantel, 50 mg/kg/day t.i.d. for 30 days</td>
<td>Albendazole, 15 mg/kg/day b.i.d. (maximum, 400 mg b.i.d.) for 8–30 days, or praziquantel, 50 mg/kg/day t.i.d. for 30 days</td>
<td>Not needed</td>
<td>Dexamethasone should be used if many CNS or subarachnoid lesions are present. Performance of an eye examination should be considered, to exclude the diagnosis of intraorbital cysts.</td>
</tr>
<tr>
<td>Schistosoma species</td>
<td>Praziquantel, 60 mg/kg/day in 2 divided doses for 1 day, or oxamniquine, 15 mg/kg once</td>
<td>Praziquantel, 60 mg/kg/day in 2 divided doses for 1 day, or oxamniquine, 15 mg/kg once</td>
<td>Not needed</td>
<td>Risk of reinfection is higher in HIV-infected people. Steroid therapy should be considered if marked edema is present.</td>
</tr>
<tr>
<td>Strongyloides stercoralis</td>
<td>Ivermectin 200 μg/kg/day for 1–2 days</td>
<td>Ivermectin 200 μg/kg/day for 1–2 days</td>
<td>Ivermectin, 200 μg/kg/day for 2 days every 2 weeks</td>
<td>For patients with hyperinfection or disseminated infection, treatment should be continued for 7–10 days or until symptoms resolve.</td>
</tr>
</tbody>
</table>

**NOTE.** Compiled from [7, 53–62]. TMP-SMZ, trimethoprim-sulfamethoxazole.
NEUROCYSTICERCOSIS

Neurocysticercosis, caused by infection with *Taenia solium*, is the most common cause of acquired epilepsy in the world and is highly endemic in all parts of the developing world where pigs are raised, especially Latin America, most of Asia, sub-Saharan Africa, and parts of Oceania [82–85]. Humans are infected by accidental ingestion of *Taenia* eggs by fecal-oral contamination [84].

Neurocysticercosis in transplant recipients is uncommon. One renal transplant recipient developed neurocysticercosis but responded to treatment with praziquantel [10]. In immunosuppressed patients, *T. solium* infection may be more prone to multiple-organ involvement [86, 87]. The effect of HIV infection on the natural history of neurocysticercosis is not fully defined. Studies of small case series have noted that basilar meningitis (racemose cysticercosis) and giant cysts, which are uncommon in immunocompetent hosts, were more common in HIV-infected patients, but no large case series have confirmed this finding [88–90].

Seizures are the most common manifestation of neurocysticercosis, but other symptoms, such as headache, hemiparesis, and ataxia, may be present and are determined by the cyst location within the neuraxis [91, 92]. Symptoms typically begin years after the initial infection, when a host inflammatory response develops against *T. solium* antigens released after the death of the parasite. Del Brutto et al. [93] proposed diagnostic criteria for neurocysticercosis that combine histologic, radiographic, immunologic, and clinical evidence. Definitive diagnosis of neurocysticercosis can be made on the basis of the following findings: (1) histopathologic evidence of neurocysticercosis, (2) a scolex within a cystic lesion visible on CT or MRI, or (3) a lesion suggestive of neurocysticercosis detected by neuroimaging or a clinical response to treatment of neurocysticercosis, combined with serologic evidence of *T. solium* infection by serum enzyme-linked immunoenlectrotransfer blot or CSF ELISA. Approximately 50% of patients with solitary intraparenchymal lesions will be seronegative, and the results of CSF ELISA are usually positive only for patients with active meningeal neurocysticercosis [94].

The drug treatment of choice for neurocysticercosis includes albendazole or praziquantel; steroids should be given concomitantly to reduce edema produced by medical treatment, especially for meningeal infection [95]. Most experts agree that the inflammatory response produced by the death of the cyst produces symptomatic neurocysticercosis and that inactive infection (i.e., presence of calcified or ring-enhancing lesions) do not require anthelminthics. If anthelminthic treatment is not indicated, seizures should be treated with anticonvulsants. Although standard treatment has been reported to be effective for immunosuppressed hosts, larger studies are required to determine the natural history of neurocysticercosis in these populations and to determine whether reconstitution of the immune system with HAART in patients with AIDS will induce more severe disease.

SCHISTOSOMIASIS (BILHARZIA)

Schistosomiasis infects up to 300 million people worldwide each year and requires an intermediate mollusk host (aquatic or amphibious snails) for completion of its lifecycle. Infection is most frequently transmitted through water contact, but transmission by organ transplantation has been described [11, 96]. Immunosuppression appears to have little effect on the natural history of schistosomiasis. For renal transplant recipients, the graft function and rate of rejection are similar regardless of whether schistosomiasis is present in the host or in the donor kidney, but recipients with schistosomiasis require higher doses of cyclosporine to achieve target blood levels and have a greater incidence of urological complications [12, 97]. For BMT recipients, veno-occlusive disease of the liver is more common in recipients with a prior history of schistosomiasis [98]. For HIV-infected people, schistosomiasis induces less granuloma formation around the egg and may predispose to a disseminated miliary infection [99]. As few cases of CNS schistosomiasis in HIV-infected people have been reported, the effect of HIV infection on the neurologic manifestations of schistosomiasis is not yet defined [100]. Although the incidence of CNS infection appears to be lower in immunosuppressed people, the lack of a host immune response may limit the development of symptomatic neurologic disease.

Acute schistosomiasis (Katayama fever) typically includes fever, urticarial swellings, myalgias, eosinophilia, and bloody diarrhea. Symptoms may last for weeks but are uncommon in populations with endemic infection [101]. Of the 5 *Schistosoma* species, 3 are capable of causing CNS infection: *Schistosoma mansoni*, *Schistosoma haematobium*, and *Schistosoma japonicum* [102]. Eggs in the CNS do not develop into worms in any mammalian host, and it is thought that adult worms do not migrate into the CNS. Due to a smaller egg size, *S. japonicum* causes 60% of all schistosomal brain infections, whereas the larger egg size of *S. mansoni* usually limits infection to the spinal cord [103]. *S. haematobium* can infect either the brain or the spinal cord [104]. After entering the CNS via the vascular system, schistosomal eggs induce a granulomatous response that eventually becomes exudative and necrotic and that can involve vascular walls [105]. Neurologic symptoms usually develop weeks or months after the initial infection. The lower spinal cord is most frequently involved in schistosomiasis and often produces symptoms of conus medullaris or cauda equina syndrome. Other reported manifestations include spinal cord compression, transverse myelitis, quadriplegia, and anterior spinal artery syndrome [22, 23].

A definitive diagnosis of CNS schistosomiasis requires the
<table>
<thead>
<tr>
<th>Infecting parasite</th>
<th>Test(s) and comment, by type of specimen</th>
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<tbody>
<tr>
<td></td>
<td>Serum</td>
</tr>
<tr>
<td>Toxoplasma gondii</td>
<td>Detection of anti–T. gondii IgG/IgM antibodies</td>
</tr>
<tr>
<td>Trypanosoma cruzi</td>
<td>Detection of anti–T. cruzi IgG/IgM antibodies; detection of trypomastigotes on Giemsa stain</td>
</tr>
<tr>
<td>Taenia solium</td>
<td>Detection of anti–T. solium IgG/IgM antibodies</td>
</tr>
<tr>
<td>Schistosoma species</td>
<td>Detection of <em>Schistosoma mansoni</em> adult microsomal antigen. Serologic testing is especially useful for patients who have a low worm burden or who have not yet started shedding eggs.</td>
</tr>
<tr>
<td>Strongyloides stercoralis</td>
<td>Detection of larvae; detection of anti–<em>S. stercoralis</em> IgG, which is especially useful if the worm burden is low and prior to shedding of eggs. Eosinophilia is usually absent during disseminated infection.</td>
</tr>
</tbody>
</table>
identification of an egg in a biopsy tissue specimen, but detection of schistosomal eggs in stool specimens (which is more sensitive for *S. mansoni*) or urine specimens (which is more sensitive for *S. hematobium*) confirms the diagnosis of schistosomiasis [106, 107] (table 4). For spinal cord infection, the use of ELISA for detection of IgG antibodies against egg antigens in CSF is recommended [108]. Neuroimaging of the brain typically reveals single or multiple hyperdense lesions surrounded by edema with variable contrast enhancement [111]. The brain may reveal a characteristic “arborized” appearance on MRI, with linear enhancement surrounded by punctate enhancing nodules [24, 112].

Praziquantel therapy is effective against all *Schistosoma* species and is curative in 60%–90% of cases [57]. Artemether, unlike praziquantel, kills immature migrating larvae (*schistosomula*), and it is synergistic with praziquantel [113]. When praziquantel is ineffective, oxamniquine may be used for treatment [114]. Antibodies often persist after anthelminthic treatment, and their presence should not be used as a measure of treatment success, but patients who continue to shed eggs in feces should be given treatment again [115, 116]. Although treatment of schistosomiasis is effective for HIV-infected people, their reinfection rate is higher than that of the general population and correlates with a lower CD4+ cell count [117]. Steroids should be added to the treatment regimen for patients with rapid neurologic decline or significant edema [111]. When large granulomas are present, surgical extirpation is usually warranted.

**STRONGYLOIDIASIS**

Strongyloidiasis, typically caused by *Strongyloides stercoralis*, was previously encountered mainly in tropical and subtropical regions. With the advent of transplantation and HIV infection, strongyloidiasis has become more prevalent worldwide [118]. Strongyloidiasis is usually acquired by direct skin contact with filariform larvae. After entering a human host, the larvae migrate to the small intestine, where the female worm lays eggs that hatch into rhabditiform larvae. The larvae are either released into the stool or molt into filariform larvae that reinfect the host, producing a chronic infection that can persist for as long as 50 years [119]. Most infections of immunocompetent hosts remain asymptomatic, although pulmonary and gastrointestinal symptoms are common during acute and chronic infection. Both hyperinfection (i.e., an increased worm burden without spread outside the gastrointestinal or pulmonary systems) and disseminated strongyloidiasis (i.e., the spread of filariform larvae to other organ systems) are more common in immunocompromised hosts [58].

With the exception of renal transplant recipients, hyperinfection and disseminated strongyloidiasis are uncommon in transplant recipients [118, 120]. The increased use of cyclosporine, which has anthelminthic properties, has reduced the incidence of strongyloidiasis in renal transplant recipients [121]. Hyperinfection and disseminated infection are uncommon in HIV-infected patients but usually occur in patients with CD4+ cell counts of <200 cells/mm³ who are concomitantly receiving corticosteroids [122]. Although strongyloidiasis hyperinfection was included in the initial Centers for Disease Control and Prevention surveillance case definitions for AIDS, it was removed from subsequent definitions because of a low occurrence rate [123]. Unexpectedly, infection with another retrovirus, human T-lymphotropic virus type 1, is frequently associated with hyperinfection and is more difficult to effectively eradicate in people with strongyloidiasis [124, 125].

Headache, altered mental status, and meningismus are the most common manifestations of CNS infection in all hosts, regardless of immune status. Myelitis and hemiparesis have also been described [25, 26, 126, 127]. Meningitis due to enteric bacteria is a complication of hyperinfection with *S. stercoralis* and may be associated with intestinal perforation or direct contamination by the larvae [27]. Neuropathologic evaluation has demonstrated the presence of larvae within capillaries, brain tissue, and meninges, but only larvae in stages of deterioration were surrounded by inflammatory reactions, which suggests that live larvae are able to elude immunosurveillance [128].

Diagnosis is usually confirmed by direct identification of larvae in stool, but testing of serial samples is recommended because of low sensitivity [109]. Larvae have also been identified in bronchial aspirates, sputum, serum, CSF, and peritoneal fluid. Detection of anti-*S. stercoralis* IgG4 antibodies by use of ELISA is sensitive but cannot distinguish between past or present infection, is crossreactive with other helminthic infections, and can give negative results in patients with disseminated infection.

Ivermectin, 200 µg/kg/day, is the treatment of choice for strongyloidiasis and, for patients with hyperinfection or disseminated infection, should be continued for at least 7–10 days or until resolution of symptoms. In immunocompromised hosts, the use of secondary prevention (e.g., a 2-day course of ivermectin every 2 weeks) may prevent hyperinfection or disseminated infection [58]. In patients receiving steroids, curative treatment is difficult and a relapse of infection is common [58]. Disseminated disease carries a mortality rate of almost 80%, so early detection and treatment are imperative [129].

**CONCLUSIONS**

Although parasitic infections are more prevalent in developing countries, they are becoming more common worldwide with the increase in international travel. Although parasitic CNS infection is uncommon, immunosuppression due to therapy after transplantation or due to HIV infection increases the risk of acquiring infection and can alter the clinical manifestations and treatment recommendations. When parasitic CNS infec-
tion of an immunosuppressed patient is suspected, the initial evaluation should include a detailed travel history and neuroimaging to guide the selection of appropriate serologic and CSF testing.

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References


